Version with Markings to Show Changes Made

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SPECIFICATION

PRODUCTION METHOD OF 1-SUBSTITUTED-1,2,3-TRIAZOLE DERIVATIVES

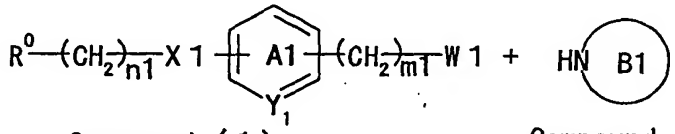
this application is a 371 of PCT/JP01/06145 filed July 16, 2001

TECHNICAL FIELD

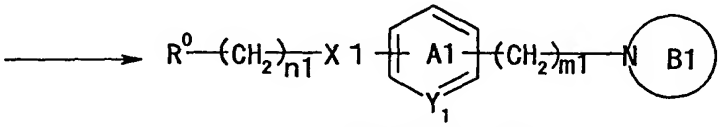
The present invention relates to production methods of intermediates for 1-substituted-1,2,3-triazole compounds having an inhibitory action on growth factor receptor tyrosine kinases (especially HER2) useful as pharmaceutical agents.

BACKGROUND ART

As a production method of an intermediate for a 1-substituted-1,2,3-triazole compound having a tyrosine kinase inhibitory action, for example, there is mentioned a method comprising condensing compound (1) of the following formula and compound (2) of the following formula in the presence of a base in a solvent inert to the reaction (e.g., aromatic hydrocarbons such as benzene, toluene, xylene etc., ethers such as tetrahydrofuran, dioxane etc., ketones such as acetone, 2-butanone etc., halogenated hydrocarbons such as chloroform, dichloromethane etc., N,N-dimethylformamide, dimethyl sulfoxide, and a mixed solvent of these) to give the objective compound (3) (JP-A-11-60571, WO 98/03505):

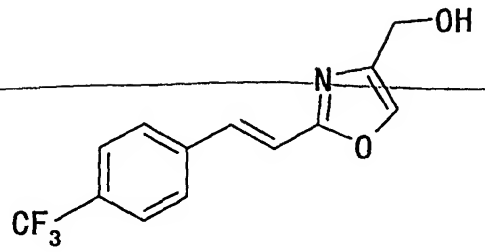


Compound (1) Compound (2)

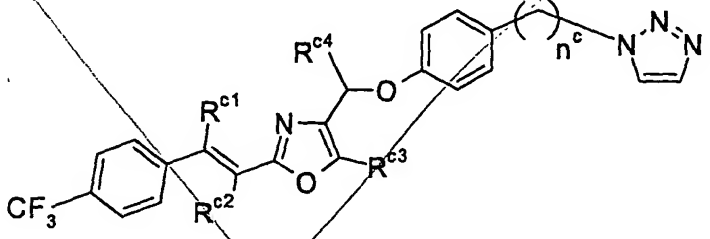


Compound (3)

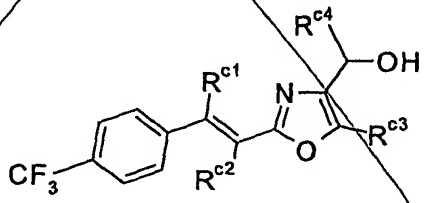
wherein W1 is a leaving group, R^0 is an optionally substituted aromatic heterocyclic group, X1 is an oxygen atom, an optionally oxidized sulfur atom, -C(=O)- or -CH(OH)-, Y_1 is CH or N, m1 is an integer of 0 to 10, n1 is an integer of 1 to 5, the cyclic group



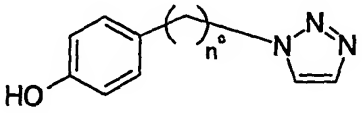
45. A method for producing a compound of the formula



wherein n^c is an integer of 1 to 10 and other symbols are as defined in claims 32, or a salt thereof, which comprises subjecting a compound of the formula



wherein each symbol is as defined above, or a salt thereof to sulfonylation or halogenation, and reacting the resulting compound with a compound of the formula



~~wherein n^c is as defined above, or a salt thereof.~~

(Amended), A crystal of

46. 1-[4-[4-[[2-[(E)-2-[4-(Trifluoromethyl)phenyl]ethenyl]-1,3-oxazol-4-yl]methoxy]phenyl]butyl]-1H-1,2,3-triazole.

~~47. The crystal of claim 46, having characteristic peaks at diffraction angles of 6.98, 14.02, 17.56, 21.10 and 24.70~~